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PTO/SB/21 (08-03)

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<b>TRANSMITTAL FORM</b>  (to be used for all correspondence after initial filing)	Application Number	10/783,780	
	Filing Date	February 20, 2004	
	First Named Inventor	Asa Abeliovich	
	Art Unit	1646	
	Examiner Name	to be assigned	
Total Number of Pages in This Submission	8	Attorney Docket Number	5199-70

ENCLOSURES (Check all that apply)		
<input type="checkbox"/> Fee Transmittal Form	<input type="checkbox"/> Drawing(s)	<input type="checkbox"/> After Allowance communication to Technology Center (TC)
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<b>SIGNATURE OF APPLICANT, ATTORNEY, OR AGENT</b>		
Firm or Individual name	Todd Holmbo, Reg. No. 42,665	
Signature		
Date	05/13/05	

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**IN THE UNITED STATES PATENT AND TRADEMARK OFFICE**

Inventor Application of: Asa Abeliovich *et al* Docket No.: 5199-70  
Serial No.: 10/783,780 Examiner: to be assigned  
Filed: February 20, 2004 Group Art Unit: 1646  
Title: PARKIN-ASSOCIATED COMPLEX FOR PROTECTING POST-MITOTIC  
NEURONS FROM EXCITOTOXICITY AND USES THEREOF

May 13, 2005

Commissioner for Patents  
P.O. Box 1450  
Alexandria, VA 22313-1450

**INFORMATION DISCLOSURE STATEMENT**  
**UNDER 37 C.F.R. §1.97(c)**

Sir:

In accordance with the duty of disclosure under 37 C.F.R. §1.56, applicant hereby notifies the U.S. Patent and Trademark Office of the following documents, which are listed on the attached PTO/SB/08B form. The examiner may deem these documents to be relevant to patentability of the claims of the above-identified application.

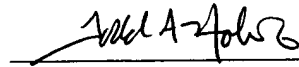
The submission of the listed documents is not intended as an admission that any of the documents constitute prior art against the claims of the present application. Applicants do not waive any right to take any action that would be appropriate to antedate or otherwise remove any listed document as a competent reference against the claims of the present application.

Applicants respectfully request that the listed documents be considered by the examiner and be made of record in the present application and that initialed a copy of form PTO/SB/08B be returned in accordance with MPEP §609.

It is understood that no fee is necessary for submission of this Information Disclosure Statement, because it is being filed before the later of three months from the filing date or the mailing of the first Office Action on the merits.

The Commissioner is hereby authorized to charge payment of any fees associated with this application or credit any overpayment to Deposit Account No. 02-4270.

Respectfully submitted,

A handwritten signature in dark ink, appearing to read "Todd A. Holmbo", is written over a horizontal line.

Todd Holmbo

Reg. No. 42,665

Attorney for Applicants

BROWN RAYSMAN MILLSTEIN

FELDER & STEINER LLP

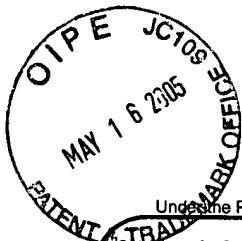
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<b>INFORMATION DISCLOSURE STATEMENT BY APPLICANT</b>  (Use as many sheets as necessary)		<b>Complete if Known</b>	
		Application Number	10/783,780
		Filing Date	02/20/2004
		First Named Inventor	Abeliovich, Asa
		Art Unit	1646
		Examiner Name	
Sheet 1	of 5	Attorney Docket Number	5199/70

NON PATENT LITERATURE DOCUMENTS			
Examiner Initials*	Cite No. <sup>1</sup>	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published.	T <sup>2</sup>
	1	Alves-Rodrigues et al., Ubiquitin, cellular inclusions and their role in neurodegeneration. Trends Neurosci., 21:516-20, 1998	
	2	Burke and Kholodilov, Programmed cell death: does it play a role in Parkinson's disease? Ann. Neurol., 44:S126-33, 1998	
	3	Carrano et al., SKP2 is required for ubiquitin-mediated degradation of the CDK inhibitor p27. Nat. Cell Biol., 1:193-99, 1999	
	4	Chung et al., Parkin ubiquitinates the alpha-synuclein-interacting protein, synphilin-1: implications for Lewy-body formation in Parkinson disease. Nat. Med., 7:1144-50, 2001	
	5	Chung et al., The role of the ubiquitin-proteasomal pathway in Parkinson's disease and other neurodegenerative disorders. Trends Neurosci., 24:S7-14, 2001	
	6	Clurman et al., Turnover of cyclin E by the ubiquitin-proteasome pathway is regulated by cdk2 binding and cyclin phosphorylation. Genes Dev., 10:1979-90, 1996	
	7	Dealy et al., Loss of Cul1 results in early embryonic lethality and dysregulation of cyclin E. Nat. Genet., 23:245-48, 1999	
	8	Dong et al., ebi regulates epidermal growth factor receptor signaling pathways in Drosophila. Genes Dev., 13:954-65, 1999	
	9	Ekholm and Reed, Regulation of G(1) cyclin-dependent kinases in the mammalian cell cycle. Curr. Opin. Cell Biol., 12:676-84, 2000	
	10	Elbashir et al., Duplexes of 21-nucleotide RNAs mediate RNA interference in cultured mammalian cells. Nature, 411:494-98, 2001	

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\*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

1 Applicant's unique citation designation number (optional). 2 Applicant is to place a check mark here if English language Translation is attached.

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**INFORMATION DISCLOSURE  
STATEMENT BY APPLICANT**

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**Complete if Known**

Application Number	10/783,780
Filing Date	02/20/2004
First Named Inventor	Abeliovich, Asa
Art Unit	1646
Examiner Name	
Attorney Docket Number	5199/70

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Examiner Initials*	Cite No. <sup>1</sup>	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published.	T <sup>2</sup>
	11	Ericson et al., Two critical periods of Sonic Hedgehog signaling required for the specification of motor neuron identity. Cell, 87:661-73, 1996	
	12	Fallon et al., Parkin and CASK/LIN-2 associate via a PDZ-mediated interaction and are co-localized in lipid rafts and postsynaptic densities in brain. J. Biol. Chem., 25:25, 2001	
	13	Hershko et al., Components of ubiquitin-protein ligase system. Resolution, affinity purification, and role in protein breakdown. J. Biol. Chem., 258:8206-14, 1983	
	14	Husseman et al., Mitotic activation: a convergent mechanism for a cohort of neurodegenerative diseases Neurobiol. Aging, 21:815-28, 2000	
	15	Hynes et al., Induction of midbrain dopaminergic neurons by Sonic hedgehog. Neuron, 15:35-44, 1995	
	16	Imai et al., An unfolded putative transmembrane polypeptide, which can lead to endoplasmic reticulum stress, is a substrate of Parkin. Cell, 105:891-02, 2001	
	17	Imai et al., CHIP is associated with parkin, a gene responsible for familial Parkinson's disease, and enhances its ubiquitin ligase activity. Mol. Cell., 10:55-67, 2002	
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	19	Joazeiro and Weissman, RING finger proteins: mediators of ubiquitin ligase activity. Cell, 102:549-52, 2000	
	20	Kamura et al., Rbx1, a component of the VHL tumor suppressor complex and SCF ubiquitin ligase. Science, 284:657-61, 1999	

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		Application Number	10/783,780
		Filing Date	02/20/2004
		First Named Inventor	Abeliovich, Asa
		Art Unit	1646
		Examiner Name	
Sheet 3	of 6	Attorney Docket Number	5199/70

NON PATENT LITERATURE DOCUMENTS			
Examiner Initials*	Cite No. <sup>1</sup>	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published.	T <sup>2</sup>
	21	Kitada et al., Mutations in the parkin gene cause autosomal recessive juvenile parkinsonism. Nature, 392:605-08, 1998	
	22	Klein et al., The harlequin mouse mutation downregulates apoptosis-inducing factor. Nature, 419:367-74, 2002	
	23	Koepp et al., Phosphorylation-dependent ubiquitination of cyclin E by the SCFFbw7 ubiquitin ligase. Science, 294:173-77, 2001	
	24	Krichevsky and Kosik, RNAi functions in cultured mammalian neurons. Proc. Natl Acad. Sci. USA, 99:11926-929, 2002	
	25	Kubo et al., Parkin is associated with cellular vesicles. J. Neurochem., 78:42-54, 2001	
	26	Lang and Lozano, Parkinson's disease. First of two parts. N. Engl. J. Med., 339:1044-53, 1998	
	27	Leroy et al., The ubiquitin pathway in Parkinson's disease. Nature, 395:451-52, 1998	
	28	Liu and Greene, Neuronal apoptosis at the G1/S cell cycle checkpoint. Cell Tissue Res., 305:217-28, 2001	
	29	Lotharius et al., Distinct mechanisms underlie neurotoxin-mediated cell death in cultured dopaminergic neurons. J. Neurosci., 19:1284-93, 1999	
	30	Matsuzawa and Reed, Siah-1, SIP, and Ebi collaborate in a novel pathway for beta-catenin degradation linked to p53 responses. Mol. Cell, 7:915-26, 2001	

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	<b>Filing Date</b>	02/20/2004
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	<b>Art Unit</b>	1646
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	31	Moberg et al., Archipelago regulates Cyclin E levels in Drosophila and is mutated in human cancer cell lines. Nature, 413:311-16, 2001	
	32	Neystat et al., Expression of cyclin-dependent kinase 5 and its activator p35 in models of induced apoptotic death in neurons of the substantia nigra in vivo. J. Neurochem., 77:1611-25, 2001	
	33	Nirenberg et al., The dopamine transporter is localized to dendritic and axonal plasma membranes of nigrostriatal dopaminergic neurons. J. Neurosci., 16:436-47, 1996	
	34	Olanow and Tatton, Etiology and pathogenesis of Parkinson's disease. Annu. Rev. Neurosci., 22 :123-44, 1999	
	35	Padmanabhan et al., Role of cell cycle regulatory proteins in cerebellar granule neuron apoptosis. J. Neurosci., 19:8747-56, 1999	
	36	Park et al., Cyclin-dependent kinases participate in death of neurons evoked by DNA- damaging agents. J. Cell Biol., 143:457-67, 1998	
	37	Patton et al., Combinatorial control in ubiquitin-dependent proteolysis: don't Skp the F-box hypothesis. Trends Genet., 14:236-43, 1998	
	38	Petrucelli et al., Parkin protects against the toxicity associated with mutant alpha-synuclein: proteasome dysfunction selectively affects catecholaminergic neurons. Neuron, 36: 1007-19, 2002	
	39	Polymeropoulos et al., Mutation in the alpha-synuclein gene identified in families with Parkinson's disease. Science, 276:2045-47, 1997	
	40	Raina et al., Cyclin' toward dementia: cell cycle abnormalities and abortive oncogenesis in Alzheimer disease. J. Neurosci. Res., 61:128-33, 2000	

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Sheet	5	of	6	Attorney Docket Number	5199/70

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	41	Scheiffele et al., Neuroligin expressed in nonneuronal cells triggers presynaptic development in contacting axons. Cell, 101:657-69, 2000	
	42	Schlossmacher et al., Parkin localizes to the Lewy bodies of Parkinson disease and dementia with Lewy bodies. Am. J. Pathol., 160:1655-67, 2002	
	43	Shimura et al., Familial Parkinson disease gene product, parkin, is a ubiquitin-protein ligase. Nat. Genet., 25:302-05, 2000	
	44	Shimura et al., Ubiquitination of a new form of alpha-synuclein by parkin from human brain: implications for Parkinson's disease. Science, 293:263-69, 2001	
	45	Singer et al., Cullin-3 targets cyclin E for ubiquitination and controls S phase in mammalian cells. Genes Dev., 13:2375-87, 1999	
	46	Skowyra et al., F-box proteins are receptors that recruit phosphorylated substrates to the SCF ubiquitin-ligase complex. Cell, 91: 9-19, 1997	
	47	Skowyra et al., Reconstitution of G1 cyclin ubiquitination with complexes containing SCFGrr1 and Rbx1. Science, 284:662-65, 1999	
	48	Spillantini et al., Alpha-synuclein in Lewy bodies. Nature, 388:839-40, 1997	
	49	Strohmaier et al., Human F-box protein hCdc4 targets cyclin E for proteolysis and is mutated in a breast cancer cell line. Nature, 413:316-22, 2001	
	50	Takada et al., Protection against dopaminergic nigrostriatal cell death by excitatory input ablation. Eur. J. Neurosci., 12:1771-80, 2000	

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	51	Troy et al., Death in the balance: alternative participation of the caspase-2 and -9 pathways in neuronal death induced by nerve growth factor deprivation. J. Neurosci., 21:5007-16, 2001	
	52	Verdaguer et al., Kainic acid-induced apoptosis in cerebellar granule neurons: an attempt at cell cycle re-entry. Neuroreport, 13:413-16, 2002	
	53	Winston et al., Culprits in the degradation of cyclin E apprehended. Genes Dev., 13:2751-57, 1999	
	54	Wu et al., Evidence for functional and physical association between Caenorhabditis elegans SEL-10, a Cdc4p-related protein, and SEL-12 presenilin. Proc. Natl Acad. Sci. USA, 95:15787-791, 1998	
	55	Wu et al., SEL-10 is an inhibitor of Notch signaling that targets Notch for ubiquitin-mediated protein degradation. Mol. Cell Biol., 21:7403-15, 2001) and presenilin	
	56	Zennou et al., The HIV-1 DNA flap stimulates HIV vector-mediated cell transduction in the brain. Nat. Biotechnol., 19:446-50, 2001	
	57	Zhang et al., Parkin functions as an E2-dependent ubiquitin- protein ligase and promotes the degradation of the synaptic vesicle-associated protein, CDCrel-1. Proc. Natl Acad. Sci. USA, 97:13354-359,	
	58	Bodansky, M., Principles of Peptide Synthesis (New York: Springer-Verlag New York, Inc., 1984 - (Not Available)	
	59	Modern Techniques of Peptide and Amino Acid Analysis (New York: John Wiley & Sons, 1981 - (Not Available)	

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